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LUNG ALERT

The ''hygiene hypothesis'' revisited

▲ Benn CS, Melbye M, Wohlfahrt J, *et al*. Cohort study of sibling effect, infectious diseases, and risk of atopic dermatitis during first 18 months of life. *BMJ* 2004;**328**:1223–7

▲ Tulic MK, Fiset P-O, Manoukian JJ, *et al*. Role of toll-like receptor 4 in protection by bacterial lipopolysaccharide in the nasal mucosa of atopic children but not adults. *Lancet* 2004;**363**:1689–97

The ''hygiene hypothesis'' suggests that decreasing exposure to micro-organisms during infancy is responsible for the increasing prevalence of atopy. However, while a decreased risk of atopic disease is associated with various surrogate markers of microbial exposure including early attendance at day care, a greater number of siblings and living on a farm, specific associations between clinical episodes of infection and atopy remain ill defined and the possible mechanisms obscure.

Two recent papers have sought to characterise further the links between infection and atopy. At a population level, Benn and colleagues used a series of four interviews to study 24 341 mother-child pairs from 12 weeks gestation until the child was 18 months old. Relationships between atopic dermatitis and the incidence of clinically apparent infections were investigated. By 6 months of age 54% of children had experienced at least one infectious episode (most commonly a cold) and at the age of 18 months 11% of the children had atopic dermatitis. While inverse correlations between the presence of atopic dermatitis and a greater number of siblings, living on a farm, pet keeping, and early day care were confirmed, the occurrence of a clinically apparent infection did not result in a decreased risk of atopy. Indeed, the risk was slightly increased. Perhaps exposure to environmental organisms in the absence of clinically apparent disease is a more important phenomenon?

At a molecular level, Tulic and co-workers report the results of a study investigating the response of ex vivo nasal mucosal samples to stimulation with allergen in the presence and absence of lipopolysaccharide (LPS). The subjects comprised 22 children and 17 adults, both with and without atopy. LPS, a major component of gram negative bacterial cell walls, interacts with host tissue via the toll-like receptor TLR-4. This provides an important link between the innate and acquired immune responses and may be one way in which exposure to micro-organisms could modulate the subsequent risk of atopy. In the presence of LPS, allergen stimulation of the nasal mucosa from atopic children (but not adults) resulted in a Th1 type response rather than the Th2 phenotype observed with allergen alone. This effect was shown to be mediated via TLR-4, with upregulation of the immunoregulatory cytokine interleukin-10. Since atopy is classically associated with a Th2 type response, the results suggest a mechanism by which exposure to microbial products might protect from atopic disease.

Debate surrounding the ''hygiene hypothesis'' continues. These two papers, rigorously conducted and using very different approaches, provide interesting insights into the possible underlying mechanisms.

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